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Introductory Chapter: A Multidisciplinary Look at Menopause

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1. Menopause as a natural process

Menopause is a natural and inevitable period of ageing in women that is well known to represent the end of reproductive life through the failure of ovarian function, accompanied by a decrease in estrogen and progestin production in the periphery and brain [1, 2]. Sexual hormones, such as estradiol and progesterone, help regulate metabolic function and interact with a wide range of neurotransmitters, such as serotonin, dopamine, λ -aminobutyric acid, and glutamate, among others [3]. Lower concentrations of these hormones during menopause have been associated with the development of specific diseases. Hormonal changes during menopause are also involved in sex differences in brain disorders that develop in aged individuals. The United States National Institutes of Health established a research priority to encourage investigations of the impact of gender on normal brain function and central nervous system-related diseases [4]. Studying menopause from a multidisciplinary perspective will help unveil different factors that affect health in this specific stage of life in women.

During menopause, lower hormone production is related to a higher incidence of vasomotor symptoms, such as hot flashes, vaginal dryness, osteoporosis, cognitive deterioration, irritability, anxiety, and mood disorders (e.g., depression) [5–8]. Menopause can occur gradually as a natural ageing process, culminating around age 50 years, or it can occur suddenly after surgical procedures, such as oophorectomy, salpingo-oophorectomy, and hysterectomy [9]. When menopause is caused by surgical manipulations, the negative symptoms can be more severe than when it occurs naturally [10]. Changes that occur during menopause interact with genetic, nutritional, sociocultural, and demographic factors [11, 12], differentially impacting quality of life in menopausal women. Research on menopause requires considerations of biology, physiology, sociology, and psychology to achieve better knowledge of this physiological

state in women and design the therapeutic approaches that focus on pharmacological treatment and psychological and physical therapy.

2. A multidisciplinary look at menopause

In this book, Dr. Kirchengast (Chapter 2) approaches menopause as a normal female stage that is a product of the overall ontogenetic and phylogenetic development of *Homo sapiens*, with a focus on evolutionary anthropology. This chapter is complemented by the work of Dr. Rovirosa-Hernández and collaborators (Chapter 3) that details the physiological changes that occur at the end of the reproductive life cycle in nonhuman primates. They compare these changes with those that are observed in menopausal women to gain a better understanding of human menopause.

Dr. Afridi Iqbal (Chapter 4) describes the ways in which psychological factors impact self-concepts and the mental health of women who experience menopause and the ways in which these factors can trigger variations in mood and such disorders as anxiety and depression.

Dr. García-Ríos and collaborators (Chapter 5) discuss the changes in serotonergic neurotransmission associated with changes in the concentrations of steroid hormones in the brain that accompany menopause and are related to greater vulnerability to depression and a lower response to antidepressant therapy in depressed menopausal women. These data are relevant when considering that aged women respond differently to antidepressants compared with young women, which could be related to lower levels of steroid hormones that negatively impact neurotransmitter function. Preclinical studies have shown that antidepressant drug treatment in middle-age ovariectomized rats that have a long-term absence of ovarian hormones is devoid of antidepressant-like effects, but if they are combined with estrogens, then an antidepressant-like effect is detected [13].

Menopause is not considered a disease but rather a natural stage of female development. However, menopause is sometimes associated with several illnesses that are associated with physical, physiological, and psychosocial factors. The most widely used treatment for menopause-related changes is hormone replacement therapy with estrogen, progestin, and their derivatives [14, 15]. Hormone replacement therapy has been shown to reduce such symptoms as bone loss, hot flashes, irritability, and mood swings [16, 17] and improve overall mental health [7]. Nevertheless, hormone replacement therapy also has side effects that restrict its long-term use in some women [18, 19]. Consequently, medicinal alternatives are needed to ameliorate menopause symptoms with a lower risk of severe side effects. Therapeutic alternatives mainly consist of dietary supplements that contain natural compounds, such as phytoestrogens, including isoflavones, flavones, lignans, coumestans, and stilbenes. Preclinical studies have shown that the phytoestrogen genistein reverses anxiety-like behavior in an experimental model of surgical menopause [20] and depression-like behavior [21].

Dr. Estrada-Camarena and collaborators (Chapter 6) describe in detail the effects of nonsteroid hormone therapy that is based on the use of natural and synthetic phytoestrogens. They

present preclinical and clinical evidence of the ways in which phytoestrogens interact with specific receptors in the brain to reduce anxiety and depression symptoms and ameliorate other illnesses that are associated with menopause.

Dr. Bittar Simoni (Chapter 7) describes the positive effects of physical activity on health in menopausal women. In his chapter, he discusses the ways in which different exercise regimens can improve body composition, functional performance, strength, and balance, thus positively impacting physical health and emotional and affective states. For example, a positive interaction has been found between estradiol concentrations and physical activity that attenuates endocrine responses to stress [22], thus decreasing irritability, anxiety, and depression symptoms.

3. Concluding remarks

Menopause is characterized by physiological, biological, and psychosocial changes that impact lifestyle and predispose them to the development of different diseases. The current therapeutic approaches are diverse, including drugs, hormones, chemical products of natural origin, meditation, and exercise, each of which have specific risks and benefits. Unfortunately, because of the complexity of the physiological and psychological changes that are associated with menopause, no completely safe and effective treatment for all symptoms has been developed.

Genetic differences can also influence the severity of symptoms and response to conventional therapies [11, 23], thus complicating the development of a general therapeutic approach for all menopausal woman. Understanding the causes of diseases that are associated with menopause and responses to different treatments should utilize a multidisciplinary approach to achieve combined therapeutic strategies for specific groups of menopausal women. Decisions regarding the treatment for menopausal women should consider symptomatology, health status, immediate and long-term health risk, personal life expectations, and the availability and cost of therapy [2]. Safer and more effective therapeutic alternatives for the management of menopausal symptoms need to be developed, specifically for women who present contraindications to hormone therapy. Although great advances have been made from psychological, physiological, pharmacological, and environmental perspectives, still much work needs to be done.

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